which stated that Applicant failed to elect a distinct species for each of the three domains of the cell membrane impermeable reagent.

As was discussed during the above-referenced telephone interview, Claim 55 recites a cell membrane impermeable reagent that is compliant with the required species election. Specifically, Claim 55 recites sulfosuccinimidyl-2-(biotinamido)ethyl-1,3-dithiopropionate as a species of cell membrane impermeable reagent. This reagent comprises the following three domains: (a) an N-hydroxysuccinimide (NHS) ester moiety (sulfosuccinimidyl), (b) a biotin binding domain (biotinamido), and (c) a cleavable chemical moiety (dithiopropionate). Accordingly, Applicant respectfully submits that the molecule recited in Claim 55 is a species election that is compliant with the Restriction Requirement mailed July 5, 2001.

CONCLUSION

In consideration of the above remarks, Applicant requests that the Notice of Non-Compliant Amendment under 37 C.F.R. §1.121 be withdrawn and that the Application be passed to Allowance.

Applicant submits that no fees are required in connection with this response, however, if additional fees are required, they may be charged to Deposit Account No. 11-1410.

Respectfully submitted,
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Dated: 2/22/02

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Claims

55. (Amended) A method of labeling a molecule exposed on a luminal surface of a perfusible space *in situ* or *in vivo* comprising the following steps:

(a) providing a cell membrane impermeable reagent comprising three domains:

(i) a first domain comprising a chemical moiety capable of covalently and non-specifically binding to a molecule exposed on the luminal surface of a cell lining a perfusible space *in situ* or *in vivo*,

(ii) a second domain comprising a labeling domain, and

(iii) a third domain situated between the first and second domains linking the first domain to the second domain by a cleavable chemical moiety, wherein the cleavable chemical moiety will not cleave under *in vivo* conditions, and further wherein the cell membrane impermeable reagent is sulfosuccinimidyl-2-(biotinamido)ethyl-1,3-[dithioproprioate] dithiopropionate; and

(b) administering the membrane impermeable reagent into the perfusible space in an intact organ or an intact animal to react the cell membrane impermeable reagent with the molecule expressed on the luminal surface of the cell lining the perfusible space to label a lumen-exposed molecule.